Complete Summary

GUIDELINE TITLE

Current diagnosis of venous thromboembolism in primary care: a clinical practice guideline from the American Academy of Family Physicians and the American College of Physicians.

BIBLIOGRAPHIC SOURCE(S)

Qaseem A, Snow V, Barry P, Hornbake ER, Rodnick JE, Tobolic T, Ireland B, Segal J, Bass E, Weiss KB, Green L, Owens DK, Joint American Academy of Family Physicians/American College of Physicians. Current diagnosis of venous thromboembolism in primary care: a clinical practice guideline from the American Academy of Family Physicians and the American College of Physicians. Ann Fam Med 2007 Jan-Feb;5(1):57-62. [45 references] PubMed

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GUIDELINE STATUS

This is the current release of the guideline.

All American College of Physicians' clinical practice guidelines are considered automatically withdrawn or invalid 5 years after publication or once an update has been issued.

COMPLETE SUMMARY CONTENT

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SCOPE

DISEASE/CONDITION(S)

Venous thromboembolism

GUIDELINE CATEGORY

Diagnosis

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Pulmonary Medicine
Radiology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To present recommendations based on current evidence to clinicians to aid in the diagnosis of lower extremity deep venous thrombosis and pulmonary embolism

TARGET POPULATION

All adults who have a probability of developing deep venous thrombosis (DVT) or pulmonary embolism, including pregnant individuals

INTERVENTIONS AND PRACTICES CONSIDERED

1. Assessment of clinical signs and symptoms
2. Estimation of probability (Wells prediction rule for diagnosing deep venous thrombosis and pulmonary embolism)
3. D-dimer assay
    - Enzyme-linked immunosorbent assay (ELISA)
    - Quantitative rapid ELISA
    - Advanced turbidimetric D-dimer determinations
4. Ultrasound
5. Contrast venography
6. Ventilation-perfusion scan
7. Multidetector helical computed axial tomography
8. Pulmonary angiography

MAJOR OUTCOMES CONSIDERED

- Morbidity
- Mortality

- Sensitivity, specificity, positive/negative predictive value, and utility of diagnostic tests

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The guideline is based on a systematic review of the evidence as detailed in a comprehensive evidence report published in 2003 and updated in the accompanying background paper by members of the Johns Hopkins University Evidence-based Practice Center (EPC) that prepared the original report. Those papers contain substantial additional detail about the evidence (see the "Availability of Companion Documents" field).

Literature Identification

EPC staff searched literature-indexing systems to identify the articles relevant to the review, including MEDLINE, EMBASE, the Cochrane Controlled Trials Register, and the Cochrane Database of Systematic Reviews. To ensure identification of all relevant articles, they examined the reference lists from material identified through the electronic searching and from discussion with experts, and reviewed the tables of contents of recent issues of the most relevant journals. For the prior evidence report, EPC staff searched for citations from the above sources through March 2002. For the current review, the search was initially extended through November 2004. As imaging technology rapidly evolves, however, the search was extended for evidence regarding computed tomography (CT) scanning and ultrasonography through June 2006.

Two members of the study team independently reviewed the titles and abstracts identified by the search to exclude those that did not meet the following eligibility criteria. For primary literature, the article described in the abstract must have been in English, addressed one of the key questions, not studied venous thromboembolism (VTE) prophylaxis only, included original human data, and not been a single-patient case report. For the review of relevant systematic reviews, the above criteria applied except the article must have included a systematic review, meta-analysis, or cost-effectiveness analysis. Additionally, data published only in abstract form were excluded. Each individual question had additional inclusion and exclusion criteria as described below. If both reviewers agreed, the abstract was included, and the full article was retrieved for review.

NUMBER OF SOURCE DOCUMENTS

In the previous systematic review, 13 systematic reviews were relevant to the questions about diagnosis of venous thromboembolism (VTE), and 27 primary

studies were relevant to these questions. In additional searching, another 18 recent studies relevant to these questions were identified.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Evidence was graded by two authors according to the Strength of Recommendation Taxonomy (SORT) developed by a consortium of editors of US family medicine and primary care journals.

Study Quality	Diagnosis
Level 1: good-quality patient-oriented evidence	Validated clinical decision rule SR/meta-analysis of high-quality studies High-quality diagnostic cohort study†
Level 2: limited quality patient-oriented evidence	Unvalidated clinical decision rule SR/meta-analysis of lower-quality studies or studies with inconsistent findings Lower-quality diagnostic cohort study or diagnostic case-control study
Level 3: other evidence	Consensus guidelines, extrapolations from bench research, usual practice, opinion, disease-oriented evidence (intermediate or physiologic outcomes only), or case series for studies of diagnosis, treatment, prevention, or screening

*Based on Strength of Recommendation Taxonomy (SORT) [Ebell MH, Siwek J, Weiss BD, Woolf SH, Susman J, Ewigman B, et al. Strength of recommendation taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. Am Fam Physician. 2004;69:548-56].

†High-quality diagnostic cohort study; cohort design, adequate size, adequate spectrum of patients, blinding, and a consistent, well-defined reference standard.

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Data Abstraction

Paired reviewers abstracted data. Evidence tables were populated with the data, and an assessment was made of the quality of the article using validated instruments, where available.

Statistical Analysis

Qualitative heterogeneity between the studies in their designs and outcomes precluded pooling the study results. Confidence intervals surrounding sensitivities and specificities were calculated assuming a binomial distribution. For the clinical prediction rule question, Receiver Operating Characteristic (ROC) curves were fitted using maximum likelihood estimation methods assuming a binormal distribution. The area under the curve was measured using ROCFIT.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

This guideline's recommendations are based on the Evidence-based Practice Centers (EPC) review, which addressed the following questions on diagnosis formulated by the American Academy of Family Physicians (AAFP) and the American College of Physicians (ACP):

- Are clinical prediction rules valuable for diagnosing deep vein thrombosis (DVT) or pulmonary embolism, and does addition of the D-dimer assay improve the test characteristics of clinical prediction rules?
- What are the test characteristics of D-dimer measurement alone when used for diagnosis or exclusion of lower extremity DVT or pulmonary embolism, and how does choice of assay affect the test characteristics?
- What are the test characteristics of ultrasonography for diagnosis of DVT, including calf vein DVT?
- What are the test characteristics of computed axial tomography (CT) for diagnosis of pulmonary embolism?

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

This guideline was approved by the American College of Physicians Board of Regents on April 4, 2006; and approved by the American Academy of Family Physicians Board of Directors on March 28, 2006.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Recommendation 1

Validated clinical prediction rules should be used to estimate pretest probability of venous thromboembolism (VTE), both deep venous thrombosis (DVT) and pulmonary embolism, and for the basis of interpretation of subsequent tests.

Good quality evidence supports the use of clinical prediction rules to establish pretest probability of disease. The Wells prediction rules for DVT and for pulmonary embolism (see Tables below) have been validated and are frequently used to estimate the probability of VTE before performing more definitive testing on patients. The Wells prediction rule performs better in younger patients without comorbidities or a history of VTE than it does in other patients. Physicians should use their clinical judgment in cases where a patient is older or presents with comorbidities.

Table 1. Wells Prediction Rule for Diagnosing Deep Venous Thrombosis: Clinical Evaluation Table for Predicting Pretest Probability of Deep Vein Thrombosis

Clinical Characteristic	Score
Active cancer (treatment ongoing, within previous 6 months, or palliative)	1
Paralysis, paresis, or recent plaster immobilization of the lower extremities	1
Recently bedridden >3 days or major surgery within 12 weeks requiring general or regional anesthesia	1
Localized tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling 3 cm larger than asymptomatic side (measured 10 cm below tibial tuberosity)	1
Pitting edema confined to the symptomatic leg	1
Collateral superficial veins (nonvaricose)	1
Alternative diagnosis at least as likely as venous thrombosis	-2

Note: Clinical probability: low $\leq$0; intermediate 1–2; high $\geq$3. In patients with symptoms in both legs, the more symptomatic leg is used.

Reprinted from *The Lancet,* Vol 350, Wells PS, Anderson DR, Bormanis J, et al. Value of assessment of pretest probability of deep-vein thrombosis in clinical management, pp 1795-8, Copyright 2002, with permission from Elsevier.

Table 2. Wells Prediction Rule for Diagnosing Pulmonary Embolism: Clinical Evaluation Table for Predicting Pretest Probability of Pulmonary Embolism

Clinical Characteristic	Score
Previous pulmonary embolism or deep vein thrombosis	+ 1.5
Heart rate >100 beats per minute	+ 1.5

Clinical Characteristic	Score
Recent surgery or immobilization	+ 1.5
Clinical signs of deep vein thrombosis	+ 3
Alternative diagnosis less likely than pulmonary embolism	+ 3
Hemoptysis	+ 1
Cancer	+ 1

Note: Clinical probability of pulmonary embolism: low 0–1; intermediate 2–6; high $\geq$7

Recommendation 2

In appropriately selected patients with low pretest probability of DVT or pulmonary embolism, obtaining a high-sensitivity D-dimer is a reasonable option, and if negative, indicates a low likelihood of VTE.

In selected patients who have a low pretest probability of VTE as defined by the Well prediction rules, a negative high-sensitivity D-dimer assay for VTE has sufficiently high negative predictive value to reduce the need for further imaging studies. Currently, enzyme-linked immunosorbent assay (ELISA), quantitative rapid ELISA, and advanced turbidimetric D-dimer determinations are highly sensitive assays (sensitivity 96% to 100%) and their use is practical in diagnosis of VTE. D-dimer testing has the highest negative predictive value when used to exclude VTE in younger patients without associated comorbidity or history of VTE and with short duration of symptoms, because the Wells criteria more accurately predict a low pretest probability of VTE in such patients. In older patients, those with associated comorbidity, and long duration of symptoms, a D-dimer alone may not be sufficient to rule out VTE.

Recommendation 3

Ultrasound is recommended for patients with intermediate to high pretest probability of DVT in the lower extremities.

Use of ultrasound in diagnosing symptomatic thrombosis in the proximal veins of the lower limb is recommended for patients whose pretest probability of disease falls in the category of intermediate to high risk of DVT under the Wells prediction rule. Ultrasound is less sensitive in patients who have DVT limited to the calf; therefore, a negative ultrasound does not rule out DVT in these patients. Repeat ultrasound or venography may be required for patients who have suspected calf-vein DVT and a negative ultrasound and for patients who have suspected proximal DVT and an ultrasound that is technically inadequate or equivocal. Contrast venography is still considered the definitive test to rule out the diagnosis of DVT.

Recommendation 4

Patients with intermediate or high pretest probability of pulmonary embolism require diagnostic imaging studies.

For patients who have intermediate or high pretest probability of pulmonary embolism, imaging is essential. Possible tests include ventilation-perfusion (V/Q) scan, multidetector helical computed axial tomography (CT), and pulmonary angiography. Recent systematic reviews indicate that CT alone may not be sufficiently sensitive to exclude pulmonary embolism in patients who have a high pretest probability of pulmonary embolism.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is specifically stated.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Early diagnosis of lower extremity deep venous thrombosis and pulmonary embolism

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- No statement in this article should be construed as an official position of the Agency for Healthcare Research and Quality or the US Department of Health and Human Services.
- Clinical practice guidelines are "guides" only and may not apply to all patients and all clinical situations. Thus, they are not intended to override clinicians' judgment.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2007 Jan/Feb

GUIDELINE DEVELOPER(S)

American Academy of Family Physicians - Medical Specialty Society
American College of Physicians - Medical Specialty Society

SOURCE(S) OF FUNDING

American College of Physicians
American Academy of Family Physicians

GUIDELINE COMMITTEE

Clinical Efficacy and Assessment Subcommittee (CEAS)

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

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GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Annals of Internal Medicine Web site.

Print copies: Available from Amir Qaseem, MD, PhD, MHA, American College of Physicians (ACP), 190 N. Independence Mall West, Philadelphia PA 19106; E-mail: aqaseem@acponline.org

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Segal J, Eng J, Tamariz LJ, Bass EB. Review of the evidence on diagnosis of deep venous thrombosis and pulmonary embolism. Ann Fam Med 2007 Jan-

Feb;5(1):63-73. Electronic copies: Available from the Annals of Family Medicine Web site.

Print copies: Available from the American College of Physicians (ACP), 190 N. Independence Mall West, Philadelphia PA 19106-1572.

- Ebell MH, Siwek J, Weiss BD, et al. Strength of recommendation taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. Am Fam Physician. 2004;69(3):548-56. Electronic copies: Available from the American Family Physician Web site.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI Institute on May 8, 2007. The information was verified by the guideline developer on May 24, 2007.

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Readers with questions regarding guideline content are directed to contact the guideline developer.

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